

~~131~~¹ A method of staining target chromosomal DNA to detect in an interphase cell one or more genetic translocations identified with chromosomal abnormalities, said method comprising:

(a) providing a heterogeneous mixture of two or more nucleic acid probes having a combined complexity of at least 40 kb, which probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that flank and/or extend partially or fully across breakpoint regions known to be associated with genetic translocations, wherein each probe comprises a distinct fluorescent label;

(b) reacting the heterogeneous mixture with the targeted chromosomal DNA by in situ hybridization; and

(c) observing the proximity or overlap of the regions stained by each probe, to determine whether said translocation is present in the interphase cell.

~~132~~² The method according to claim ~~131~~¹, wherein the translocation is associated with a cancer.

~~133~~³ The method according to claim ~~132~~², wherein said cancer is CML and a first probe is substantially complementary to at least a part of a BCR gene on chromosome 22 and a second probe is substantially complementary to at least a part of a ABL gene on chromosome 9.

~~134~~⁴ The method according to claim ~~133~~³, wherein the BCR probe comprises 18 kb and comprises part of, and extends centromeric to, the 5.8 kb breakpoint cluster region of the BCR gene.

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~~135.~~ The method according to claim ~~133~~³, wherein the ABL probe

comprises 35 kb and is telomeric to the 200 kb region of ABL between exons IB and II.

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136. ~~The method~~ according to claim 133, wherein the ABL probe and the
BCR probe are hybridized to the chromosome and are separated by from about 25 to about

└ 225 kb.

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~~137.~~ The method according to claim ~~133~~³, wherein the BCR probe is
labeled with biotin and the ABL probe is labeled with dioxigenin.

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~~138.~~ The method according to claim ~~133~~³, wherein the BCR probe is
labeled with dioxigenin and the ABL probe is labeled with biotin.

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139. The method according to claim 133, wherein the BCR hybridization
complex and the ABL hybridization complex are no more than 1 micron from each other.

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~~140.~~ The method according to claim ~~131~~⁹, further comprising adding
blocking nucleic acid that comprises fragments which are substantially complementary to
repetitive segments in the targeted chromosomal DNA.

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~~141.~~ The method according to claim ~~131~~¹⁰, wherein the hybridization
capacity of repetitive segments of the nucleic acid is disabled.

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~~142.~~ The method according to claim ~~131~~¹¹, wherein the probes are labeled
such that a dual color fluorescence is produced.

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~~143.~~ The method according to claim ~~131~~¹², wherein the translocation is
associated with Burkitts lymphoma.

144. The method according to Claim 131, wherein said probes have a combined complexity of between about 40 and 750 kb.

145. The method according to claim 144, wherein said probes have a combined complexity of between about 50 and 400 kb.

~~146.~~¹⁵ The method according to claim ~~131~~¹, wherein said probe is labeled with a direct label or an affinity label.

~~147.~~¹⁶ A method of distinguishing normal and malignant cells comprising staining target chromosomal DNA to detect in an interphase cell one or more genetic translocations identified with chromosomal abnormalities of malignant cells, said method comprising:

(a) providing a heterogeneous mixture of two or more nucleic acid probes having a combined complexity of at least 40 kb, which probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that flank and/or extend partially or fully across breakpoint regions known to be associated with genetic translocations, wherein each probe comprises a distinct fluorescent label;

(b) reacting the heterogeneous mixture with the targeted chromosomal DNA by in situ hybridization;

(c) observing the proximity or overlap of the regions stained by each probe to determine whether said translocation is present in the interphase cell, wherein said translocation is indicative of a malignant cell.

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~~148.~~ A method of determining prognosis for a patient and/or determining the effectiveness of a therapy comprising staining target chromosomal DNA to detect in an interphase cell one or more genetic translocations identified with chromosomal abnormalities of malignant cells, said method comprising:

(a) providing a heterogeneous mixture of two or more nucleic acid probes having a combined complexity of at least 40 kb, which probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that flank and/or extend partially or fully across breakpoint regions known to be associated with genetic translocations, wherein each probe comprises a distinct fluorescent label;

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(b) reacting the heterogeneous mixture with the targeted chromosomal DNA by in situ hybridization;

(c) observing the proximity or overlap of the regions stained by each probe to determine whether said translocation is present in the interphase cell, wherein the occurrence of a translocation is indicative of the prognosis of the patient and/or the effectiveness of therapy.

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~~149.~~ A method according to claim ¹⁷~~148~~, wherein the therapy is selected from the group consisting of chemotherapy, radiation, surgery and transplantation.

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150. A method of staining target chromosomal DNA to detect in an interphase cell one or more genetic translocations identified with chromosomal abnormalities, said method comprising:

(a) providing a heterogeneous mixture of two or more nucleic acid probes having a combined complexity of at least 40 kb, which probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that flank and/or extend partially or fully across breakpoint regions known to be associated with genetic translocations;

(b) reacting the heterogeneous mixture with the targeted chromosomal DNA by in situ hybridization;

(c) adding a distinct fluorescent label to said nucleic acid probes; and

(d) observing the proximity or overlap of the regions stained by each probe, to determine whether said translocation is present in the interphase cell.

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~~151.~~ The method according to claim ¹⁹~~150~~, wherein said label is a direct label or an affinity label.

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~~152.~~ The method according to claim ¹⁹~~150~~, wherein one of said nucleic acid probes is labeled with biotin.

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~~153.~~ The method according to claim ¹⁹~~150~~, wherein one of said nucleic acid probes is labeled with dioxigenin.

REMARKS

Entry of the foregoing, reexamination and reconsideration of the above-identified application are respectfully requested.